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Therapy of patients with human T-cell lymphotrophic virus I-induced adult T-cell leukemia with anti-Tac, a monoclonal antibody to the receptor for interleukin-2.

Blood. 1988 Nov;72(5):1805-16. Unique Identifier : AIDSLINE MED/89027118

Waldmann TA; Goldman CK; Bongiovanni KF; Sharroo SO; Davey MP; Cease KB; Greenberg SJ; Longo DL; Metabolism Branch, National Cancer Institute, Bethesda, MD 20892.

Abstract: Human T-cell lymphotropic virus I (HTLV-I)-induced adult T-cell leukemia (ATL) cells constitutively express interleukin-2 (IL-2) receptors identified by the anti-Tac monoclonal antibody (MoAb), whereas normal resting cells do not. This observation provided the scientific basis for a trial of intravenous anti-Tac in the treatment of nine patients with ATL. The patients did not suffer untoward reactions and did not have a reduction in the normal formed elements of the blood, and only one of the nine produced antibodies to the anti-Tac MoAb. Three patients had transient mixed, partial, or complete remissions lasting from 1 to more than 8 months after anti-Tac therapy, as assessed by routine hematologic tests, immunofluorescence analysis of circulating cells, and molecular genetic analysis of HTLV-I provirus integration and of the T-cell receptor gene rearrangement. The precise mechanism of the antitumor effects is unclear; however, the use of a MoAb that prevents the interaction of IL-2 with its receptor on ATL cells provides a rational approach for the treatment of this malignancy.

Keywords: Adult Antibodies, Monoclonal/*THERAPEUTIC USE Female Gene Rearrangement, beta-Chain T-Cell Antigen Receptor Human Immunotherapy Leukemia-Lymphoma, T-Cell, Acute, HTLV-I-Associated/BLOOD/GENETICS/*THERAPY Male Middle Age Receptors, Interleukin-2/*IMMUNOLOGY T-Lymphocytes/IMMUNOLOGY/PHYSIOLOGY JOURNAL ARTICLE

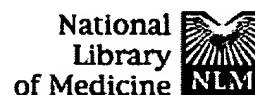
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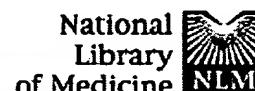
Human T-cell lymphotropic virus I (HTLV-I)-induced adult T-cell leukemia (ATL) cells constitutively express interleukin-2 (IL-2) receptors identified by the anti-Tac monoclonal antibody (MoAb), whereas normal resting cells do not. This observation provided the scientific basis for a trial of intravenous anti-Tac in the treatment of nine patients with ATL. The patients did not suffer untoward reactions and did not have a reduction in the normal formed elements of the blood, and only one of the nine produced antibodies to the anti-Tac MoAb. Three patients had transient mixed, partial, or complete remissions lasting from 1 to more than 8 months after anti-Tac therapy, as assessed by routine hematologic tests, immunofluorescence analysis of circulating cells, and molecular genetic analysis of HTLV-I provirus integration and of the T-cell receptor gene rearrangement. The precise mechanism of the antitumor effects is unclear; however, the use of a MoAb that prevents the interaction of IL-2 with its receptor on ATL cells provides a rational approach for the treatment of this malignancy.

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The interleukin-2 receptor: a target for monoclonal antibody treatment of human T-cell lymphotrophic virus I-induced adult T-cell leukemia.

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Waldmann TA, White JD, Goldman CK, Top L, Grant A, Bamford R, Roessler E, Horak ID, Zaknoen S, Kasten-Sportes C, et al.

Metabolism Branch and Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892.

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Adult T-cell leukemia (ATL) is a malignancy of mature lymphocytes caused by the retrovirus human T-cell lymphotrophic virus-I (HTLV-I). It is an aggressive leukemia with an overall mortality rate of 50% within 5 months; no conventional chemotherapy regimen appears successful in inducing long-term disease-free survival in ATL patients. However, ATL cells constitutively express high-affinity interleukin-2 receptors (IL-2Rs) identified by the anti-Tac monoclonal antibody, whereas normal resting cells do not. To exploit this difference in receptor expression, we administered anti-Tac intravenously (IV) to 19 patients with ATL. In general the patients did not suffer untoward reactions, and in 18 of 19 cases did not have a reduction in normal formed elements of the blood. Seven patients developed remissions that were mixed (1 patient), partial (4 patients), or complete (2 patients), with partial and complete remissions lasting from 9 weeks to more than 3 years as assessed by routine hematologic tests, immunofluorescence analysis, and molecular genetic analysis of T-cell receptor gene rearrangements and of HTLV-I proviral integration. Furthermore, remission was associated with a return to normal serum calcium levels and an improvement of liver function tests. Remission was also associated in some cases with an amelioration of the profound immunodeficiency state that characterizes ATL. Thus the use of a monoclonal antibody that blocks the interaction of IL-2 with its receptor expressed on ATL cells provides a rational approach for treatment of this aggressive malignancy.

MeSH Terms:

- Adult
- Antibodies, Monoclonal/therapeutic use*
- Antineoplastic Combined Chemotherapy Protocols/therapeutic use
- Blotting, Southern
- Female
- Follow-Up Studies
- Gene Rearrangement, T-Lymphocyte
- Human
- Human T-lymphotropic virus 1/genetics

- Leukemia-Lymphoma, T-Cell, Acute, HTLV-I-Associated/drug therapy
- Leukemia-Lymphoma, T-Cell, Acute, HTLV-I-Associated/genetics
- Leukemia-Lymphoma, T-Cell, Acute, HTLV-I-Associated/immunology*
- Leukemia-Lymphoma, T-Cell, Acute, HTLV-I-Associated/therapy*
- Male
- Middle Aged
- Receptors, Interleukin-2/immunology*
- Restriction Mapping
- Virus Integration

Substances:

- Antibodies, Monoclonal
- Antineoplastic Combined Chemotherapy Protocols
- Receptors, Interleukin-2

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TA Waldmann, CK Goldman, KF Bongiovanni, SO Sharro, MP Davey, KB Cease, SJ Greenberg and DL Longo

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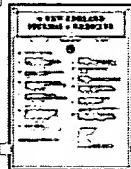
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